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| 10/609,346 | 06/26/2003 | Zailin Yu | ZYU-0603 | 1103 |
| 7590 | 08/24/2006 | | EXAMINER | |
| FortuneRock Inc. Attn: Dr. Zailin Yu Apt. D109 3120 Saint Paul St. Baltimore, MD 21218 | | | MERTZ, PREMA MARIA | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1646 | |
| DATE MAILED: 08/24/2006 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding..

| | | | |
|------------------------------|----------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/609,346 | YU ET AL. | |
| | Examiner Prema M. Mertz | Art Unit 1646 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 14 July 2006.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 21-23,27-33,40 and 41 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 21-23, 27-33, 40-41 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II (claims 21-23, 27-33, 40-41) in the reply filed on 7/14/2006 is acknowledged. Claims 1-11, 15-20, 24-26, 34-39, 42-50 have been canceled (6/16/2006) and claims 12-14 have been canceled (7/14/2006).

Claims 21-23, 27-33, 40-41, are pending and under consideration by the Examiner.

Claim rejections-35 USC § 112, first paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 21-23, 27-33, 40-41, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid having at least 90%, and 95% nucleotide sequence identity with a particular disclosed sequence (SEQ ID NO:7). The claims do not require that the polynucleotide encoding the polypeptide possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides encoding polypeptides that is defined only by sequence identity. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include

disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved for the biological activity of the protein. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics and structure/function relationship, the specification does not provide adequate written description of the claimed genus.

Vas-cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only a nucleic acid encoding a polypeptide of amino acid sequence set forth in SEQ ID NO:8 as recited in claim 23, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

2b. Claims 21-23, 27-33, 40-41, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide of amino acid sequence set forth in SEQ ID NO:8, does not reasonably provide enablement for an isolated nucleic acid having at least 90%, and 95% nucleotide sequence identity with a particular disclosed sequence (SEQ ID NO:7). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 21, for example, is overly broad in its limitation of “at least 90% sequence identity” because no guidance is provided as to which of the myriad of nucleic acid molecules encompassed by the claims will encode a polypeptide which retains the characteristics of the desired polypeptide. Variants of a nucleic acid can be generated by deletions, insertions, and substitutions of nucleotides, but no actual or prophetic examples on expected performance parameters of any of the possible variants of the claimed nucleic acid molecule or muteins of the protein molecule have been disclosed. Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human

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glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate and use a nucleic acid having at least 90%, and 95% nucleotide sequence identity with SEQ ID NO:7 other than the polynucleotide of SEQ ID NO:7 exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by

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the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of the claims, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-23, 27-33, 40-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21, is vague and indefinite because it recites “comprising: a nucleotide sequence at least....” rather than “comprising a nucleotide sequence....”.

Claim 27, line 2, is vague and indefinite because it recites “specific antibody of human albumin”. It is unclear what this term means.

Claim 28, is vague and indefinite because it recites “comprising: the sequence of the polynucleotide....” rather than “comprising the polynucleotide”.

Claim 31 is vague and indefinite because it recites “but not limited, *Saccharomyces....*” rather than “but not limited to *Saccharomyces....*”.

Claim 32 is vague and indefinite because it is incomplete. Furthermore, the claim if complete would be a duplicate of claim 31. It is suggested that this claim be deleted.

Claims 22-23, 29-30, 33, 40-41 are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 21-23, 27-33, 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shaw (4,904,584) in view of the Capon et al. patent (U.S. Patent No. 5,116,964).

The Shaw patent discloses a polynucleotide encoding a human G-CSF protein, vectors for recombinant vectors for expression of the protein and host cells for producing the recombinant protein (see abstract; column 1, lines 5-14; columns 10-12, Examples 1, 2 and 3). A comparison of the amino acid sequence presented in Figure 4 of the Shaw patent with the amino

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acid sequence of G-SCF presented in Figure 1(H) of the instant application supports the conclusion that the G-CSF protein of Shaw patent is the same as the G-CSF polypeptide of the instant invention. However, Shaw does not disclose a polynucleotide encoding both G-CSF and albumin to obtain a fusion protein comprising albumin and G-CSF to increase the half-life of the G-CSF.

Capon et al. teaches chimeric proteins for directing ligand binding partners such as growth factors, hormones or effector molecules to cells bearing ligands for the ligand binding partners comprising a ligand binding partner fused to a stable plasma protein which is capable of extending the *in vivo* half-life of the ligand binding partner when present as a fusion with the ligand binding partner, in particular wherein such a stable plasma protein is an immunoglobulin constant domain or albumin (see column 4, lines 57-64; column 5, lines 11-21; column 7, lines 11-27; column 8, lines 13-15).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art to modify the polynucleotide of Shaw such that it includes both, the polynucleotide encoding G-CSF and the polynucleotide encoding albumin, to obtain a chimeric protein with an increased circulating half-life, as taught by Capon et al., to obtain the known functions and advantages of the G-CSF polypeptide as per the teachings of Shaw. Cytokines such as G-CSF are well-known in the art as having a short half-life. One would have been motivated to use a chimeric polynucleotide encoding a chimeric protein comprising G-CSF and albumin to decrease the clearance rate of G-CSF *in vivo*. Therefore, it would have been obvious to obtain a chimeric polynucleotide encoding G-CSF and albumin, a long-lived molecule well known in the art as able to increase the stability of rapidly cleared molecules.

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Conclusion

No claim is allowed.

Claims 21-23, 27-33, 40-41, are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz
Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
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